11th February 2021

Direct Healthcare Professional Communication

AmBisome Liposomal 50 mg Powder for dispersion for infusion (PL 16807/0001): identify and dispose of co-packaged Sartorius 5µm Minisart Filters due to potential to release fibres during use

Dear Pharmacist,

Gilead in agreement with the Medicines and Healthcare products Regulatory Agency would like to inform you of the following:

Summary

- Defective Minisart 5µm sterile filters co-packaged with AmBisome batches listed in the Appendix may release fibres and particles into the infusion, which could pose a risk of causing thromboembolism in the patient receiving liposomal amphotericin
- There is no quality issue associated with AmBisome product and due to supply considerations, the product is not being recalled
- Although the risk is considered to be of low clinical relevance and no adverse reports have been received to date, if thromboembolism does occur it would be of high severity, particularly in paediatric patients
- Pharmacists should follow the instructions below to identify affected stocks in pharmacy and clinical settings and to dispose of the defective Minisart filters provided in the cartons; alternative filters are available
- Inform all relevant healthcare professionals within your hospital of the information in this letter and return the confirmation form to Gilead

Actions requested of pharmacists immediately

1. Check the existing stock within your hospital and identify if any of the AmBisome lots listed in Appendix 1 are in your hospital. Please note that in addition to the pharmacy, this includes clinics, wards (adults and paediatric units) and any other relevant locations within your hospital.
2. Open the cartons and remove the defective Minisart® 17594-GJR filters (see Appendix 2 for image example of Sartorius filter) and ensure you dispose of them appropriately. These filters should not be used.

3. Other suitable 5 micron filters may be available in your hospital. Alternatively, as stated under section 6.6 of AmBisome SmPC: "An in-line membrane filter may be used for intravenous infusion of AmBisome. However, the mean pore diameter of the filter should not be less than 1.0 micron".
4. Filters from an alternative supplier are available from Gilead. Please contact your Gilead Customer Services representative at UKCustomer.Services@gilead.com if you require information concerning suitable alternative filters or if you require replacement filters.
5. Complete Page 7 of this letter and send it to UKIEproductcomplaints@gilead.com.

Background to the safety concern

AmBisome (Liposomal Amphotericin B) is indicated for use in children from 1 month of age and in adults for the treatment of severe systemic and/or deep mycoses; visceral leishmaniasis in immunocompetent patients; and the empirical treatment of presumed fungal infections in febrile neutropenic patients, where the fever has failed to respond to broad spectrum antibiotics and appropriate investigations have failed to define a bacterial or viral cause. AmBisome is provided with filters for dilution and transfer into the dextrose infusion bag.

Gilead has been notified of a quality defect issue by our supplier, Sartorius, in relation to specific lots of 5µm sterile filters, which are co-packed in cartons of the AmBisome product. The medical device is called *Minisart® Filter 17594-GJR*. Sartorius has informed Gilead that the filter lots packaged with the AmBisome batches listed in the Appendix may be releasing fibres and particles, which may pose a risk to the patient.

From a risk perspective, a preliminary Health Hazard Evaluation performed by Gilead has assessed the risk of thromboembolism associated with the use of AmBisome with the affected filters in the indicated populations. The severity of harm (if risk occurs) is considered high, because the quality defect could potentially result in permanent impairment of body function or permanent damage to a body structure (e.g. lungs). AmBisome is indicated in patients aged 1 month and older. The paediatric population is at greatest risk, and the quality defect is considered potentially life-threatening in this population.

The likelihood of clinically relevant occurrence of the risk is considered low, given the small size of the identified particulates and the short-term anticipated period of exposure to AmBisome. No evidence of increased adverse reaction reporting of either infusion-related reactions or thromboembolic events has been identified. While this does not confirm an absence of clinical sequelae, it supports the Gilead assessment that the overall probability of adverse health consequences is low.

If you have supplied this product to any other pharmacy or clinic, please send a copy of this notice to them and request the above instructions are followed.

Call for reporting

Please continue to report suspected adverse drug reactions (ADRs) to the MHRA through the Yellow Card Scheme.

Please report:

- all suspected ADRs that are serious or result in harm. Serious reactions are those that are fatal, life-threatening, disabling or incapacitating, those that cause a congenital abnormality or result in hospitalisation, and those that are considered medically significant for any other reason
- all suspected ADRs associated with new drugs and vaccines identified by the black triangle ▼

Report via:

- the Yellow Card website www.mhra.gov.uk/yellowcard
- the free Yellow Card app available from the Apple App Store or Google Play Store
- some clinical IT systems (EMIS/SystmOne/Vision/MiDatabank) for healthcare professionals

Alternatively, you can report a suspected side effect to the Yellow Card scheme by calling 0800 731 6789 for free, Monday to Friday between 9am and 5pm. You can leave a message outside of these hours.

When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset, treatment dates, and product brand name.

Any suspected adverse reactions should be reported to Gilead via email to Safety_FC@gilead.com and IEproductcomplaints@gilead.com or by telephone +44 (0) 1223 897500.

Further Information
For more information or medical information queries, please contact:
Gilead Sciences Ltd Medical Information
Telephone: +44 (0) 8000 113700
E-mail: ukmedinfo@gilead.com

For stock control queries, please contact:
Customer Care direct line: +44 (0)203 681 4681
E-mail: UKCustomer.Services@gilead.com

Please do not hesitate to contact us should you have any queries on this notification.

Yours sincerely,

Julian Cole,

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UK & Ireland Senior Director, Medical Affairs

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Yours sincerely,

Katriona Methven,

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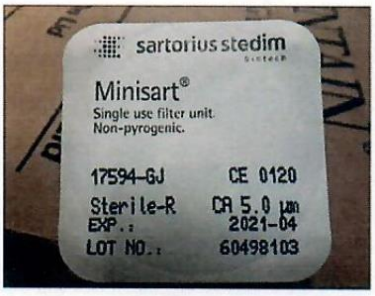
APPENDIX 1

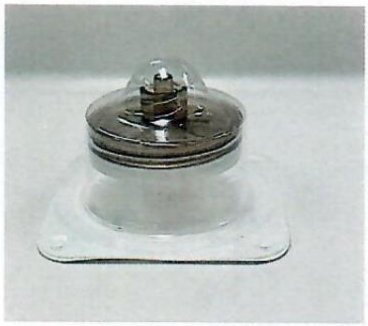
List of impacted AmBisome lots

Lot Number	Expiry Date
019364D	31-Aug-23
D1900146D	31-Oct-23
019545D	30-Nov-23
GAD221D	31-Dec-23
020759D	29-Feb-24
019547D	30-Nov-23
D2000038D	31-Mar-24
020570D	31-May-24
GAD244D	30-Apr-24
020595D	31-Dec-23
D2000066D	31-May-24
D2000049D	30-Apr-24

APPENDIX 2

Image example of Sartorius filter





Hospital/Doctor Name

<Address>

<Address>

<Address>

For the attention of:

UKIEproductcomplaints@gilead.com

Gilead Sciences Ltd
280 High Holborn
London WC1V 7EE
United Kingdom

Dear Sir/Madam,

I confirm that relevant staff in our pharmacy have read and understood the Gilead Notice dated February 11th 2021 in relation to the withdrawal of Sartorius filters in packs of AmBisome, that all relevant healthcare professionals in our hospital responsible for the administration of AmBisome will be informed of that Notice, and that the filters present in the cartons of AmBisome for any AmBisome lots listed in the Appendix to the Notice will be disposed of.

Completed by:	
Name: (please print name)	
Position:	
Hospital:	

Signed: _____ Date: _____